Topology-Guided Multi-Class Cell Context Generation for Digital Pathology

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Introduction
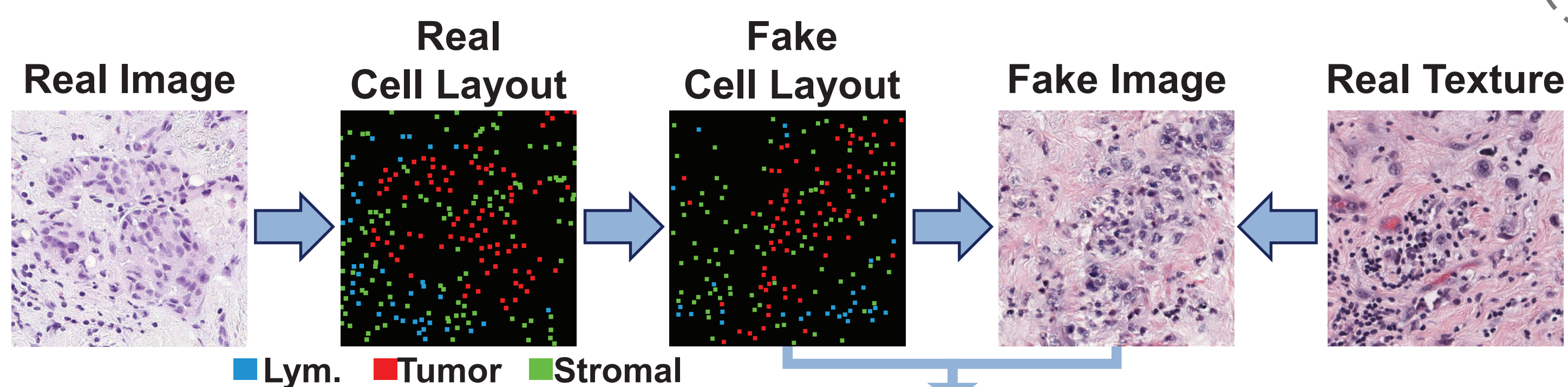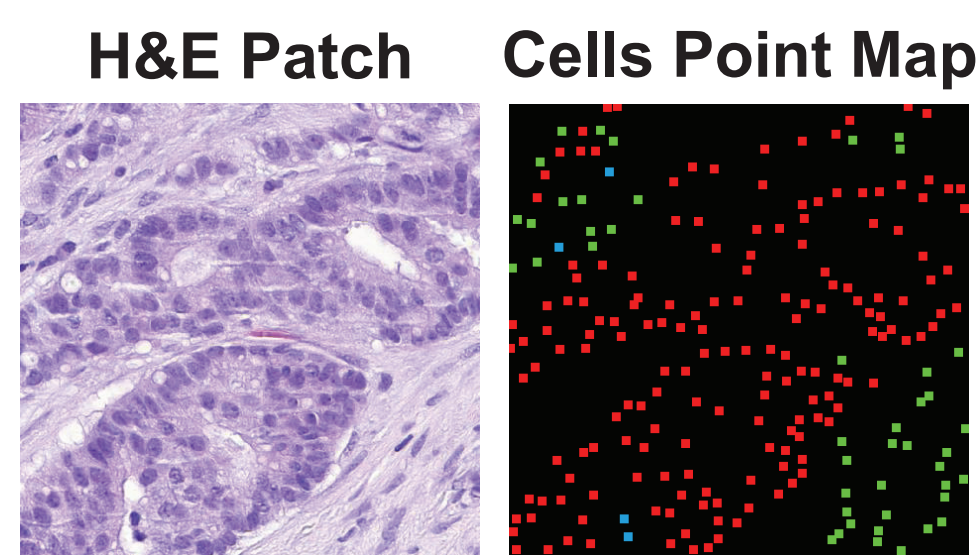
Pathology image analysis suffers from **limited annotations**!

➡ *Solution:* **Augment** training **with generated labeled** data.

Generating pathology images usually involves **two steps**:

1. Generating spatial layout of cells. — **Our Focus**

2. Filling in stains and textures.

Cell Context

• The **arrangement** of cells.

• Their **spatial co-localization.**

• **Important** for pathology data analysis.

H&E Patch   **Cells Point Map**

Real Image → **Real Cell Layout** → **Fake Cell Layout** → **Fake Image** ← **Real Texture**

■Lym. ■Tumor ■Stromal

Train Downstream Tasks

Challenges: • **Complexity** of the cell layout.

• *How to model* and learn the underlying distribution.

We introduce mathematical descriptors to model and learn the *spatial distribution* of *multi-class* cells and their *structural patterns*.
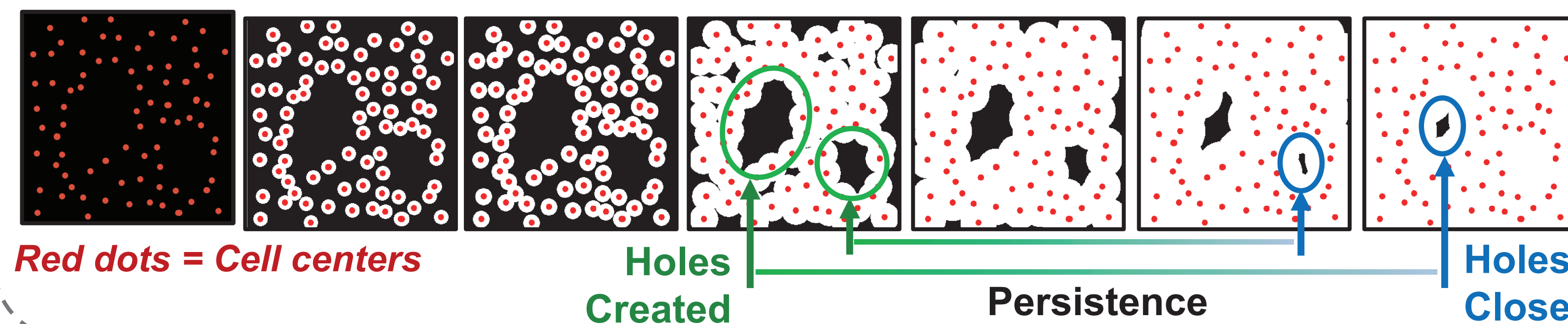
Cell Configuration Descriptors

1. Topological Features

Clusters

Holes

Persistence Diagram
Death / Birth

Persistent Homology Filtration ➡ **Persistence Diagram (PD)**

Red dots = Cell centers

Holes Created — **Persistence** — **Holes Close**

2. Spatial Statistics Features

• **Cell types co-localization**

• **Characterize neighborhoods of holes**

$K(r)$, r_{i+1}, c_i, r_i
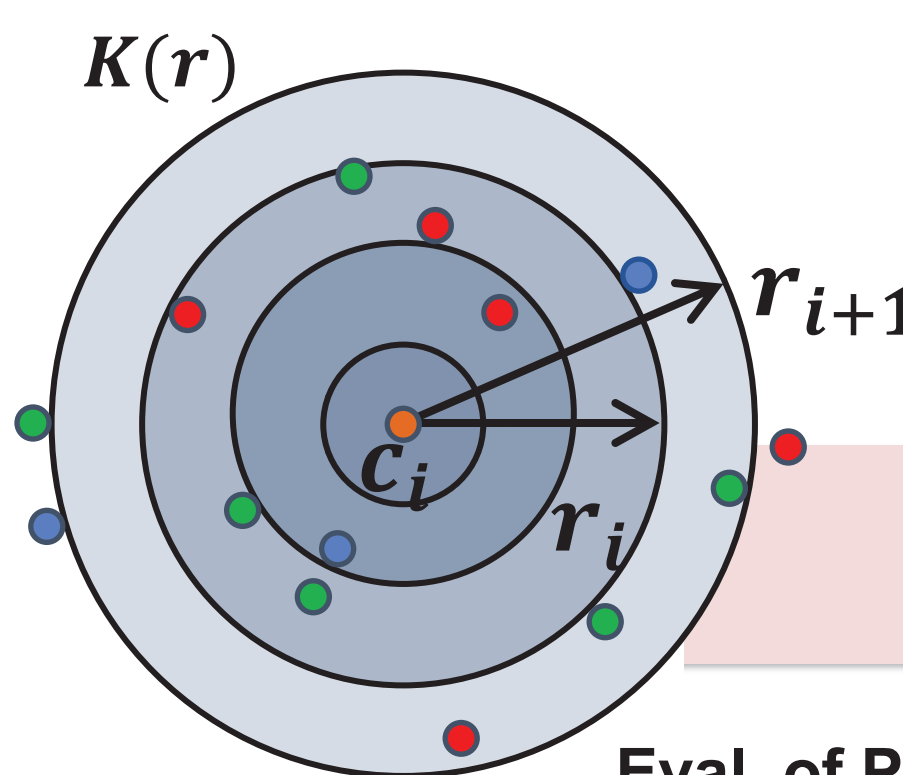
Ripley's K / Cross-K function

$K(r)$

Clustered

K-function of rand. process and its confidence interval

An observed K-function
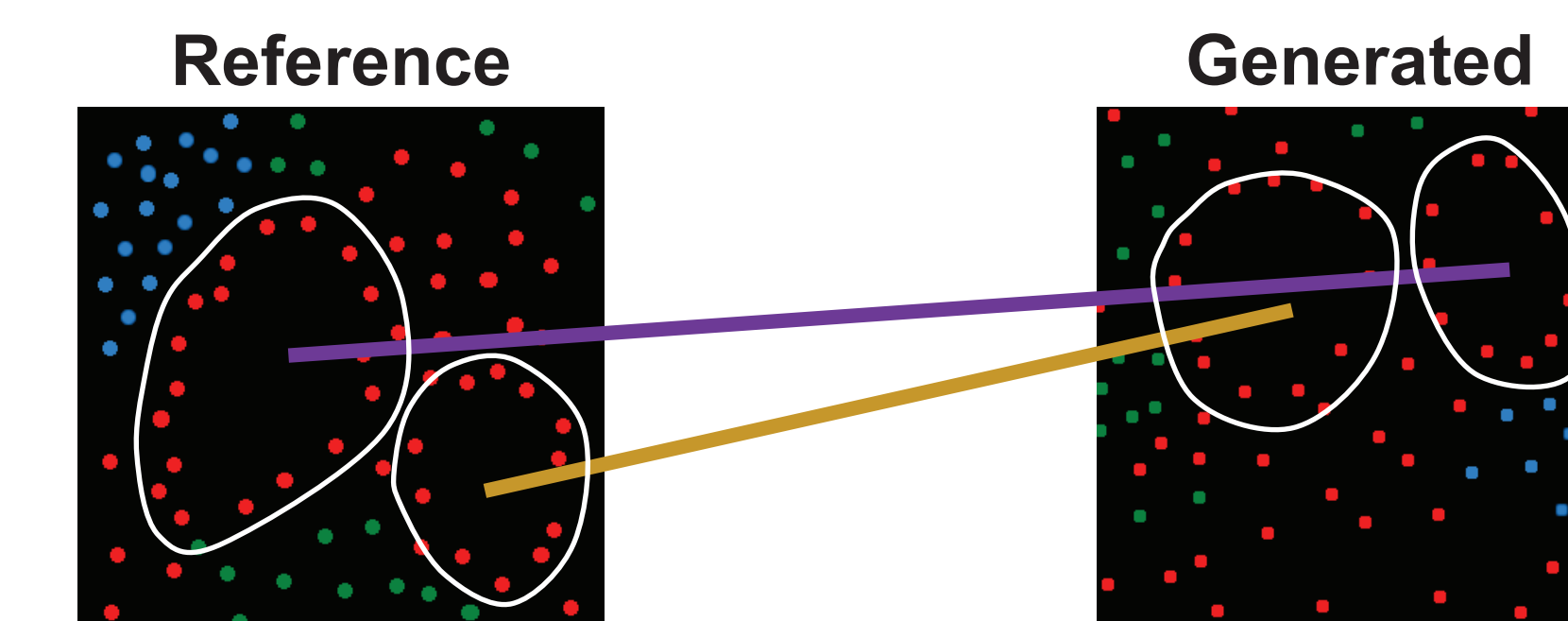
Dispersed

$radius\ r$
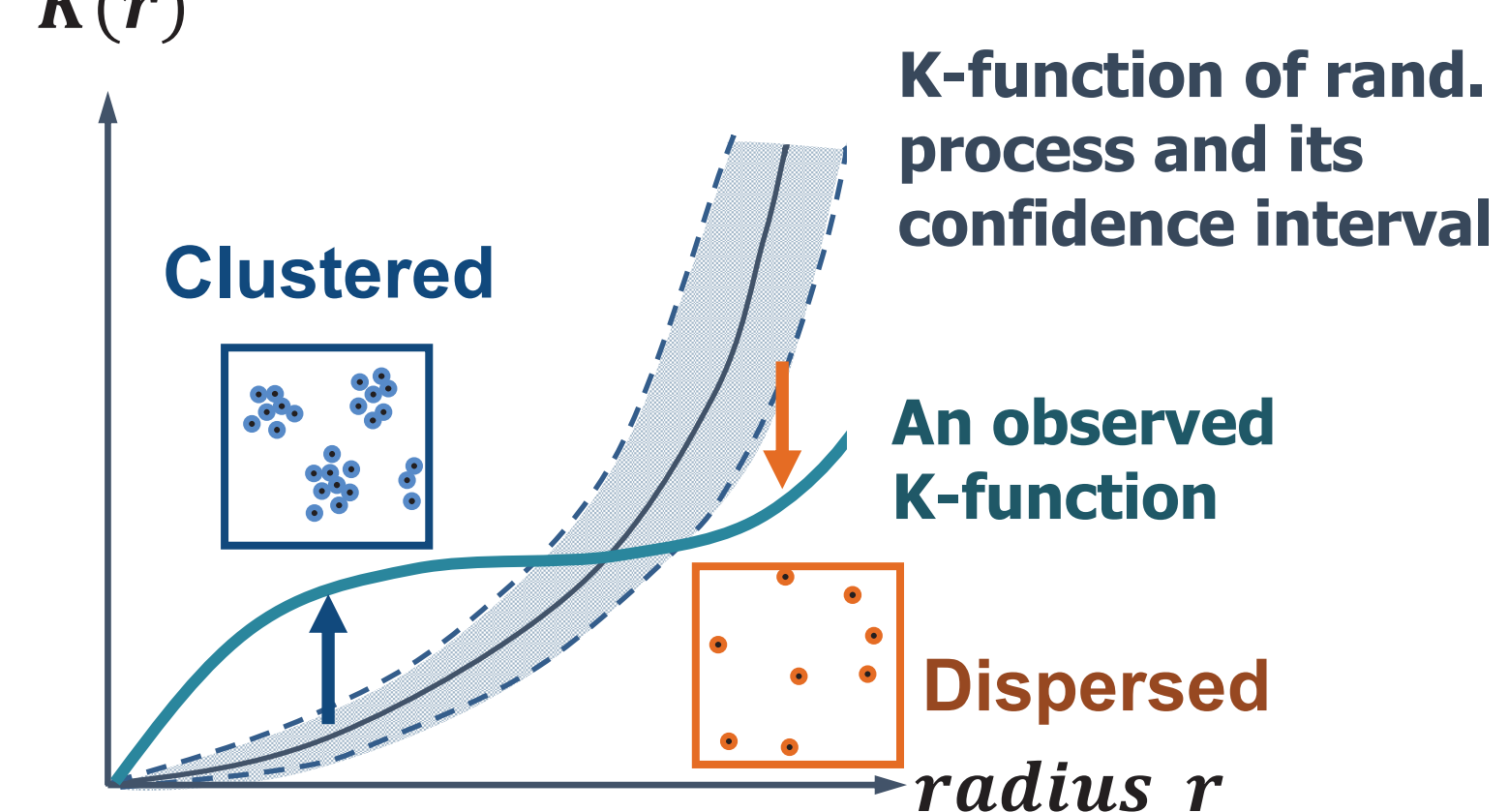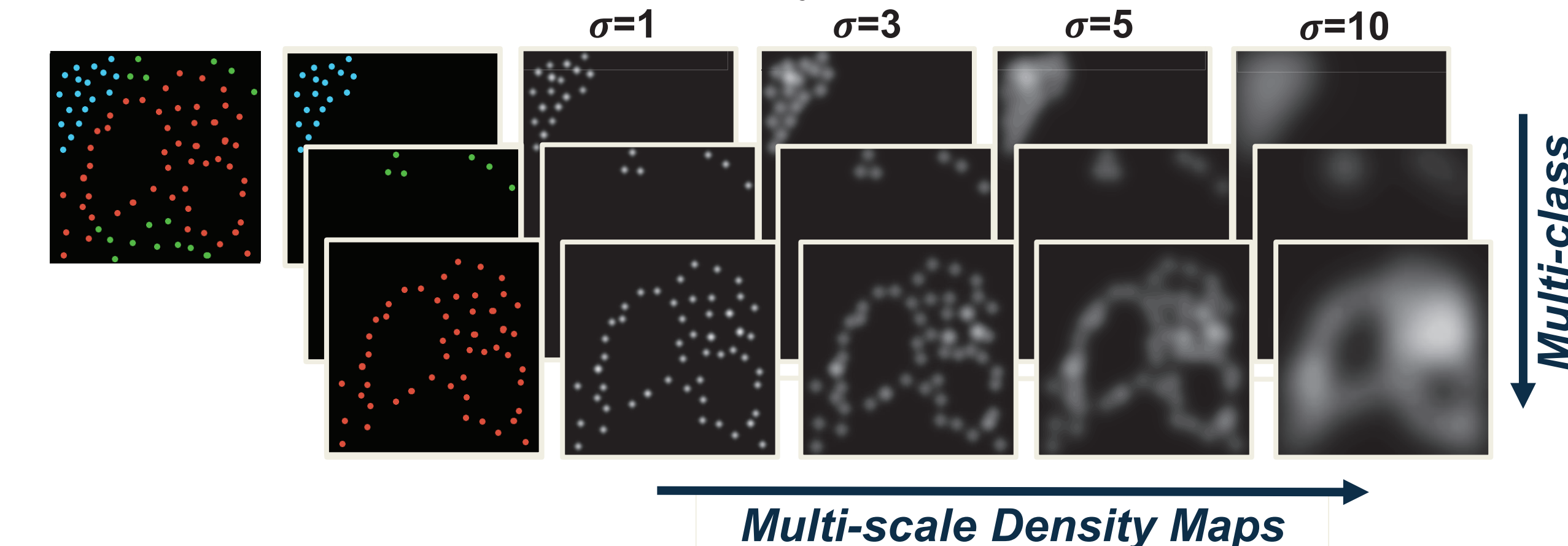
Model Backbone: A modified version of SPGAN*

* Li et al. SP-GAN: sphere-guided 3d shape generation and manipulation. SIGGRAPH, 40(4), 2021.

Cell Configuration Loss $\mathcal{L}_{cc}$

Match holes based on::
size (*persistence*), and spatial context (*cross K functions*)

Reference   **Generated**

Minimize distance between density values at matched locations

$\sigma=1$ $\sigma=3$ $\sigma=5$ $\sigma=10$

Multi-class

Multi-scale Density Maps

Results

Eval. of Persistence Diagrams (Cell Config. Matching)↓

Method	Lym.	Tumor	Stro.	Mean
w/o Spatial Descriptors + w/o $\mathcal{L}_{cc}$	0.8	1.74	1.66	1.4
w/o $\mathcal{L}_{cc}$	0.9	1.69	1.79	1.46
w/o Cross K-function Descriptor	0.75	1.74	1.77	1.42
Ours	0.74	1.64	1.71	**1.36**

Eval. on Cell Classification (F-Score)↑

Method	Lym.	Tumor	Stro.	Mean
U-Net	0.498	0.744	0.476	0.572
U-Net + Aug. (Rand.)	0.625	0.735	0.472	0.611
U-Net + Aug. (Ours)	**0.65**	**0.768**	**0.511**	**0.644**

Sample Generated Cell Layouts

Real Cells' Layout

Generated Cells' Layout